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| EXAMINER | |
|---|---|
| EPPS FORD, JANET L | |
| ART UNIT | PAPER NUMBER |
| 1633 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/540,743 | STEWART ET AL. | |
| | Examiner | Art Unit | |
| | Janet L. Epps-Ford | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *38-74* is/are pending in the application.

4a) Of the above claim(s) *59,60,64 and 66-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-58,61-63 and 65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of group I, claims 38-58, 61-63, and 65 in the reply filed on 7-02-08 is acknowledged. The traversal is on the ground(s) that there would be no serious burden on the examiner to search all the inventions of Groups I-III together. This is not found persuasive because as stated in the prior Office Action, the inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features. The technical relationship shared among Groups I-III, namely methods comprising encapsulating cells in the presence of an integrin binding partner, does not make constitute a special technical relationship since it does not make a contribution over the prior art. Thus the inventions of Groups I-III lack unity of invention for the reasons set forth in the original requirement for restriction.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 59-60, 64, and 66-74 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7-02-08.

3. Claims 38-58, 61-63, and 65 are pending for examination.

### *Claim Rejections - 35 USC § 112*

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 39-44 and 63 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

7. In the present instance, claim 39, and those claims dependent therefrom, claims 40-44, recite the broad recitations of "collagen" and "collagens," and further recites "type 1 collagen," which is a narrower statement of the limitation collagen or collagens. Additionally, claim 39 recites the term "factor X" is duplicated at line 3, and at line 6.

8. In the present instance, claim 63 recites the broad recitation progenitor/stem cells, and the claim also recites "e.g. from bone marrow, adipose, or peripheral blood," which is the narrower statement of the range/limitation.

***Claim Rejections - 35 USC § 102***

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 38-39 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Ramdi et al. (1993).

11. Claim 38 recites a method of preparing a prepared cell, comprising encapsulating said cell in a cell encapsulation medium in vitro to form an encapsulation product for use in cell therapy in vivo, wherein said encapsulation product includes an integrin binding partner; claim 39 is drawn to wherein the integrin binding partner is collagen, Fibronectin, fibrinogen..., and claim 41 recites wherein the binding partner is fibronectin.

12. Ramdi et al. (1993; See Search Report of WO 2004/058305 A3), describes an encapsulation methodology that is carried out in the presence of an integrin binding partner, namely type I collagen, type IV collagen, and fibronectin (as defined by instant claim 39). See page 451, 2nd col., for the following:

*Entrapped Cells*

*Cell proliferation kinetics.* Cell proliferation
carried out in each case as described under Materi
and Methods. Immobilized cells were cultured wit
alginate matrices loaded with the same adjuvants as
monolayers. Representative growth curves are show
Fig. 4. For all the cultures we noticed an increasing
sponse over time with a short lag period at Day 1. Ma
ces with type I collagen, type IV collagen, or type(I + I
collagen + fibronectin appeared to constitute the
propriate conditions for cell proliferation. They allow
for an exponential response from Days 1 to 4.

Ramdi et al. (1993), clearly reads on instant claims 38-39 and 41.

13. Claims 38-39, 41, 44-52, 55-58, 63, and 65 are rejected under 35 U.S.C. 102(b) as being anticipated by Schinstine et al. (US Patent No. 5,776,747).

Schinstine et al. teach a method for the encapsulation of cells comprising in one or more embodiments the following methods:

"According to one method, a suitable cell is transformed with a gene encoding a differentiation-inducing product. This differentiation-inducing gene is operatively linked to a regulatable promoter. According to this method, the differentiation-inducing gene would be expressed upon *encapsulation* and in vivo implantation in a host." (col. 11, lines 1-7)

"In another embodiment according to this invention, cells seeded on microcarriers may be suspended in the presence of a suitable growth-inhibiting matrix and then *encapsulated* in the BAO. Such matrix material (e.g., *agarose or agar for fibroblasts; collagen for adrenocortical cells*) physically inhibits further cell outgrowth. Such hydrogel matrices are described..."

"According to another aspect of this invention, agarose may also be used as a substitute for ECM by derivatization with peptide sequences to affect cell attachment to the matrix. For example, agarose hydrogels may be derivatized with peptide sequences of laminin or fibronectin." (anticipates claim 50)

"In this method, *cells are suspended in 3-D matrices composed of agarose derivatized with a peptide sequence that recognizes a cell surface receptor molecule involved in cell adhesion*. Several peptide sequences have been shown (in 2-D) to promote cell adhesion.....The derivatized agarose matrices of this invention allow presentation of the appropriate molecular cues for cell adhesion in 3-D. The agarose concentration is preferably 1.25% w/v or less, most preferably about 1.0%. We prefer RGD-containing sequences (i.e. ArgGlyAsp; AA.sub.2 -AA.sub.4 of SEQ ID NO:2), YIGSR-containing sequences (TyrIleGlySerArg; AA.sub.5 -AA.sub.9 of SEQ ID NO:1), IKVAV-containing sequences (IleLysValAlaVal; AA.sub.11 -AA.sub.15 of SEQ ID NO:3), and the like. Derivatization can be achieved using a bi-functional coupling agent, such as 1'1, carbonyldiimidazole or any other suitable method." (col. 17, lines 1-37).

The above passages clearly teach the use of a derivatized matrix of agarose comprising an integrin binding partner laminin or firbronectin, and wherein the agarose is derivatized with an RGD containing sequence. Furthermore, this passage suggests that the integrin binding partner is bound to the cell prior to encapsulation. Thus the above passage anticipates claims 38-39, 41, 44, 46, 48-49.

Moreover, this reference teaches that "[a]garose is a clear, thermoreversible hydrogel made of polysaccharides.....Agarose can be chemically modified by derivatives, e.g., polyethylene oxide-poly (dimethyl siloxane) (PEO-PDMS), to further inhibit cell

outgrowth, preferably without toxic effects to the cells." (col. 17, lines 53-56). This passage is considered to anticipate claims 51-52 since both agarose (natural) and derivatized forms of agarose (synthetic) are useful as an encapsulation medium.

Schinstine et al. also teach methods for controlling cell growth by the modification of the surface of an bioartificial organ (BAO) by chemically attaching RGD peptides to the surface, wherein cells are encapsulated within the BAO, however the encapsulation medium would not contain the RGD modification. See, col. 18, which sets forth the following: "For example, RGD (ArgGlyAsp; AA.sub.2 -AA.sub.4 of SEQ ID NO:2), the most common of these peptides can be chemically attached to the BAO membrane, using known techniques. Some RGD (ArgGlyAsp; AA.sub.2 -AA.sub.4 of SEQ ID NO:2) containing molecules are commercially available……In another embodiment, the BAO membrane can be modified to inhibit cell attachment through adsorption of, e.g., PEO-PDMS or poly(d-lysine)-alginate. We prefer PEO-PDMS modification, particularly if the growth surface is porous. This is because PEO-PDMS will tend to diffuse through the pores and adsorb to the surface as it passes through the pores through hydrophobic-hydrophobic bonding. In particular, low molecular weight (600-3000 g/mole) PEO-PDMS is preferred. *This embodiment is particularly useful when cells are grown on microcarriers and encapsulated in the BAO. In this manner, an even cell distribution may be achieved, cell number may be controlled, and cell adhesion may be limited to the microcarrier."*

Schinstine et al. is interpreted to encompass wherein the integrin binding partner is not bound to the prepared cell to the extent that the surface of the agarose or the BAO

membrane can be chemically modified to inhibit cell attachment by the attachment of PEO-PDMS. (claim 47).

***Claim Rejections - 35 USC § 103***

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 38-58, 61-63, and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schinstine et al.

16. The teachings of Schinstine et al. are incorporated here. However Schinstine et al. does not specifically teach wherein the integrin binding protein is fibrinogen, FXIII, or FXIIIa. Additionally, this reference does not specifically teach wherein the encapsulation product contains one cell.

It would have been obvious to the ordinary skilled artisan to modify the methods of Schinstine et al. to comprise the use of alternative integrin binding partners such as fibrinogen, Factor XIII or Factor XIIIa. Since the prior art recognizes the use of integrin binding partners in the preparation of cells for encapsulation, the ordinary skilled artisan would have had a reasonable expectation of success of substituting the prior art integrin binding partners with a functionally equivalent integrin binding partner with the expectation of

producing similar results, specifically for use in the encapsulation of cells. See MPEP § 2144.06[R-6].

In regards to the claims directed to the encapsulation of one cell, absent evidence to the contrary, since the general parameters of the claimed invention was known in the art, and the claimed invention differs only by the number of cells encapsulated, variations in the number of encapsulated cells in the prior art method is merely a difference in design choice. Regarding the rationale for combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Primary Examiner, Art Unit
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*JLE*